

REMARKS

Claims 1-12, 14, 19-22, 32-51, 54-56, 58, and 59 are currently pending. Claims 32-40, 44-51, 54-56, 58, and 59 are withdrawn from consideration at this time. Claims 1-12, 14, 19-22, and 41-43 stand rejected. With this response, Applicants amend claims 1, 14, 20, 32, 43, 47, 56, and 58. Claims 7-10 and 21-22 are cancelled. Each of the rejections levied in the Office Action is addressed individually, below.

Rejection of claim 43 under 35 U.S.C § 112, first paragraph.

Claim 43 is rejected under 35 U.S.C § 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the claim “contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” Specifically, the Examiner states “said claims are rejected due to claiming a conjugate associate[d] with a diagnostic agent.” Applicants respectfully traverse the Examiner’s assertion and direct the Examiner’s attention to page 66, paragraph [0196] of the application as filed, which describes conjugates associated with a diagnostic label as well as exemplary diagnostic labels. In order to expedite prosecution, Applicants amend claim 43 to replace the term “agent” with “label,” and respectfully request that the Examiner withdraw the rejection.

The Examiner also asserts that “how the claimed conjugate associates with the diagnostic agent is not described and defined.” Applicants respectfully traverse and submit that the specification provides more than sufficient description of claimed conjugates comprising a carrier with one or more modifiers. In addition, Applicants direct the Examiner’s attention to page 28, paragraph [0049] of the application as filed for an explicit definition of the term “associated with.” In view of the ample teachings in the specification, Applicants respectfully request that the Examiner withdraw the rejection.

Rejection of claims 7 and 10 under 35 U.S.C § 112, second paragraph.

Claims 7 and 10 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for “failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Specifically, the Examiner asserts that the use of the word “derivatives” in claims 7 and 10 renders the claim indefinite because “the specification does not define as the essential elements of the parent substance.” Applicants respectfully traverse, and submit that one of ordinary skill in the art would understand the use of the term “derivatives” as recited in claims 7 and 10. Solely in order to expedite prosecution, Applicant have cancelled claims 7 and 10 for reasons explained below. Applicants respectfully request that the rejection be removed.

Rejection of claims 1-2, 5, 7-10, and 41 under 35 U.S.C § 102(b).

Claims 1-2, 5, 7-10, and 41 are rejected under 35 U.S.C § 102(b) as being anticipated by Cervigni *et al.*, *Angew. Chem. Int. Ed. Engl.*, (1996), 35(11), pp. 1230-1232 (“Cervigni”). The Examiner asserts that “Cervigni *et al.* disclosed an oxime-containing conjugate [that] anticipates the instant claimed invention. Since the said conjugate is claimed for biological application, the composition comprising said conjugate thereof is also anticipated.” Applicants respectfully traverse.

As an initial matter, Applicants amend claim 1 to recite that “the carrier comprises a biodegradable biocompatible polymer selected from polyacetals or polyketals;” With this new recitation, claims 7-10 and 21-22 are cancelled to avoid improper dependency from amended claim 1. For the record, this amendment is made for the sole purpose of expediting prosecution of this case. Applicants explicitly reserve the right to pursue claims to this subject matter, including claims of identical scope to those cancelled here, in other filings.

Applicants respectfully submit that Cervigni contains no disclosure or teaching of an oxime-containing conjugate comprising a polymeric carrier selected from polyacetals or polyketals, and therefore the reference cannot anticipate Applicants’ claimed conjugates.

Specifically, the presently amended claims are drawn toward conjugates wherein a pharmaceutically useful modifier is conjugated via an oxime linkage to a polymeric carrier selected from polyacetals or polyketals. Applicants respectfully submit that the constructs disclosed by Cervigni are simple glycopeptides or lipopeptides. Applicants respectfully point out that Cervigni describes the ligation of peptides to “aldehyde-containing compounds such as carbohydrates and lipids,” and characterizes the technique as offering “a variety of possibilities for modulating the physical, chemical, and biological properties of peptides.” In contrast to the instantly claimed conjugates, the constructs disclosed by Cervigni are merely chimeric conjugates of a peptide with a lipid, steroid, saccharide, PEG, or peptide. Because Cervigni does not disclose or teach polymeric carriers selected from polyacetals or polyketals, Applicants respectfully submit that the Cervigni reference cannot anticipate the instantly claimed conjugates, and request that the rejection be removed.

Rejection of claims 1-12, 14, 19-22, and 41-43 under 35 U.S.C § 103(a).

Claims 1-12, 14, 19-22, and 41-43 are rejected under 35 U.S.C § 103(a) as unpatentable over Cervigni *et al.*, in view of U.S. Patent No. 5,958,398 by Papisov (“the ‘398 patent”), U.S. Patent No. 5,612,037 by Huebner (“the ‘037 patent”), and G. Hermanson, Preparation of Liposome Conjugates and Derivatives, Bioconjugate Techniques, pp. 552-589, (“Hermanson”). The Examiner states that “Cervigni *et al.* teach an oxime conjugate of a carrier and modifier, but do not teach all the specific carrier such as polyketal as in claims 12 and 14; maleimide- or N-hydroxysuccinimide ester containing crosslinker as in claims 3 and 4; or a liposome based carrier.” The Examiner indicates that such differences would have been obvious to one skilled in the biochemistry and medicinal chemistry arts over the combined teachings of the ‘398 patent, the ‘037 patent, and Hermanson. Applicants respectfully traverse.

Applicants respectfully point out that, as recited in the MPEP § 2143, “to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation . . . to modify the reference . . . Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all of the claim

limitations.” For the reasons set forth below, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

First, Applicants respectfully submit that the Examiner has failed to show that Cervigni offers any suggestion or motivation to modify the disclosed constructs. As stated above, Cervigni does not teach a conjugate of a carrier and modifier as presently claimed, but rather shows only the synthesis of glycoproteins or lipoproteins, wherein the function of the complete construct is unspecified. Furthermore, Cervigni offers no suggestion to use an oxime linkage to conjugate peptides to pharmaceutically suitable carriers, nor does Cervigni suggest making conjugates wherein the pharmaceutically useful component is anything less than the entire construct itself.

Second, even if one of ordinary skill were motivated to modify the Cervigni by conjugation to a polyacetal carrier as taught in the ‘398 patent, the Examiner has failed to show there would be a reasonable expectation of success within the references. The teachings, suggestions, and expectation of success must come from the prior art, not Applicants’ disclosure. See In re Vaack, 947 F.2d 488, 493 (Fed. Cir. 1991). Cervigni suggest conjugation only to aldehyde-containing compounds such as carbohydrates, lipids, steroids, PEG, or peptides, the reference does not suggest conjugation to polyacetals or polyketals. Polyacetals such as those described in the ‘398 patent are susceptible to nucleophilic attack, and the overall integrity of the polymers can be compromised under acidic conditions in the presence of nucleophiles such as the amino-oxy reagents used by Cervigni to form oximes. Therefore, due to potential stability issues with the carriers of the ‘398 patent when using the techniques of Cervigni, there would not have been a reasonable expectation of success when setting out to prepare the claimed conjugates.

Furthermore, Applicants respectfully submit that the ‘037 patent teaches away from the Applicants’ claimed invention. Specifically, the ‘037 patent teaches conjugates of HA protein suitable for “obtaining a strong immune response to the HA protein,” and that “conjugate molecules so produced may be purified and employed in immunogenic compositions as vaccine materials to elicit, upon administration to a host, an immune response to the HA protein which is

potentiated in comparison to HA alone.” None of the instantly claimed carriers are designed to potentiate an immune response to a modifier compared to the modifier alone. In fact, certain of the present carriers are specifically designed to attenuate or mitigate an immunogenic response (see, for example, page 76, paragraph [0227]). While an antigenic modifier may be used, carriers that function to increase the immunogenic response of the modifier are not a part of the claimed invention.

The Examiner asserts that Hermanson, in combination with Cervigni and the ‘398 patent, renders the present claims obvious. Applicants respectfully traverse and submit that Hermanson does not remedy the defects in Cervigni. Indeed, and as acknowledged by the Examiner, “the lipid/liposome carriers are taught and or suggested by Hermanson for biological applications.” Specifically, Hermanson only teaches liposomes conjugated to antibodies, biotinylated compounds, or other proteins. Thus, there is no teaching, motivation, or suggestion from Hermanson to modify Cervigni to arrive at the present amended claims.

For all of these reasons, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to claims 1-12, 14, 19-22, and 41-43 and respectfully request that the Examiner withdraw the rejection.

Double Patenting

Claims 1-12, 14, 19-22, and 41-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 29-42 of copending U.S. Pat. Appl. No. 10/501,565 (the ‘565 application).

Applicants respectfully submit that the rejection of claims 1-12, 14, 19-22, and 41-43 under the judicially created doctrine of obviousness-type double patenting is premature because no claim of the ‘565 application has been patented. In view of the provisional nature of this rejection, Applicants hold this rejection in abeyance to be addressed when a relevant claim of the ‘565 application issues. Accordingly, Applicants respectfully request that the Examiner

withdraw the rejection of claims 1-12, 14, 19-22, and 41-43 and acknowledge patentability of the same.

Miscellaneous Amendments

In order to more accurately point out Applicants' invention, Applicants amend claims 1, 20, 32, 47, 56, and 58 to replace "biologically active" with "pharmaceutically useful."

Claim 14 is amended to correct a typographical error.

No new matter has been added.

Applicants invite the Examiner to call their agent, Andrea L. C. Robidoux, at (617) 248-5124 with any questions pertaining to the above-identified application in order to expedite prosecution of this case.

Respectfully submitted,

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